Properties of Free Films Prepared from Aqueous Polymers by a Spraying Technique

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A spray method for the preparation of free films from aqueous polymeric dispersions was investigated. Free films were prepared from aqueous dispersions of methacrylic acid-ethyl methacrylate copolymer (Eudragit® L 30D), hydroxypropyl methylcellulose acetate succinate (HPMCAS), cellulose acetate phthalate (CAP), and ethyl cellulose (EC) by a spray method and a cast method, and their mechanical properties and reproducibility were investigated. Uniform films were obtained from the dispersions of Eudragit® L 30D, HPMCAS, and EC by the spray method, but films could not be formed by spraying the CAP dispersion. The tensile strength, elongation, and elastic modulus of the sprayed Eudragit® L 30D films were similar to the properties of the cast films, and good reproducibility was obtained from both methods. Marked within-run variation in the mechanical properties was observed for the cast HPMCAS and CAP films, which could be due to a settling of the solid particles during the drying step. The variation in the mechanical properties of the sprayed HPMCAS films was lower and the tensile strength significantly higher than that of the cast films. There were also significant differences in tensile strength and elongation of EC films between products of the two methods. The results indicated that the spray method used to prepare the free films from aqueous polymeric dispersions provided uniform films with consistent and reproducible properties.

KEY WORDS: films; Eudragit® L 30D; hydroxypropyl methylcellulose acetate succinate; cellulose acetate phthalate; ethyl cellulose; aqueous polymeric dispersion.

INTRODUCTION

During the past decade, many pharmaceutical companies around the world have been interested in aqueous coating technology for both environmental and economic reasons. Several types of film-forming polymers have been used for film coating of solid oral dosage forms. Film coating has successfully been utilized to protect the dosage form from gastric fluid, to control the release of active ingredients, and to prevent interaction between ingredients. Film coating has also increased the strength of the dosage form to maintain product integrity during shipping. The composition of coating formulations usually contains many additives in addition to the polymer, and in most formulations, plasticizers are included to add flexibility to the films. Pigments are added for appearance, and lubricants are used to prevent adhesion. Numerous kinds of polymer blends for controlled-release formulation have been investigated. The physical-mechanical property of coating films is an important characteristicwhich helps to predict the stability and release property of film-coated dosage forms and also provides information concerning possible interactions between the components in the coating films. Such studies are usually conducted with free films.

Several studies on the physical and mechanical properties of pharmaceutical coating polymers using free films have been reported (1-6). In most of these studies, free films were prepared by casting either aqueous or organic polymeric solutions and dispersions. The properties of free films prepared from the water soluble polymer, hydroxypropyl methylcellulose (HPMC), have been reported by several researchers (1–3). Kildsig *et al.* (1) reported on the physical properties of hydroxypropyl methylcellulose free films. Johnson *et al.* (2) studied the effect of plasticizers on properties of these films. The permeation and mechanical characteristics of free films of HPMC have been reported by Okhamafe and York (3).

In addition to water-soluble polymers, aqueous formulations containing water-insoluble polymers for enteric coating and controlled-release applications have also been developed to replace organic solvent systems. Bindschaedler *et al.* (4) reported on water transport through cellulose acetate membranes produced from a latex system. Muhammad *et al.* (5) carried out an evaluation of hydroxypropyl methylcellulose phthalate films cast from aqueous dispersions. The mechanical properties of films from aqueous ethyl cellulose dispersion have been investigated by Guo *et al.* (6). Studies on aqueous acrylic resins using free films have been carried out by Bodmeier and Paeratakul (7,8). Lin *et al.* (9) also reported on the mechanical properties and plasticizer compatibility with polymeric dispersions of an acrylic resin. Gutiérrez-Rocca and McGinity (10) studied the aging effect on the physical-mechanical properties of free films from aqueous acrylic dispersions. In all the literature mentioned above, the free films were prepared by casting aqueous or organic polymeric dispersions or solutions. However, cast methods have presented several problems. In formulations containing solid particles, sedimentation may occur during the drying stages, resulting in non-uniform films. The preparation of multiple-layered films by the cast method is also difficult, since the solvent present when casting secondary layers may dissolve or interact with earlier layers.

A spray method which yields uniform and reproducible free films would be ideal for evaluating polymers that are currently used in coating, especially in light of the problems mentioned above. Allen *et al.* (11) reported a methodology to prepare free films by a spray method using an apparatus with a rotary cylinder. A similar method has been reported by Van Bommel *et al.* (12–14). Both studies were based on an organic solvent system. In 1989, Li and Peck (15) carried out an evaluation of an aqueous latex of a silicone elastomer with free films prepared by a spray method. Goodhart and coworkers (16,17) studied the softening temperatures of free films that were prepared by spraying aqueous polymeric dispersions onto Teflon® plates.

Although the spray method will generate a film that is more representative of that formed during film coating, numerous technical problems must be circumvented in order to prepare reproducible films. Few researchers have reported

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on the use of spraying techniques to prepare free films from aqueous polymeric solutions or dispersions (18). The objectives of this study were to develop methodologies for preparing uniform free films of aqueous pharmaceutical polymeric dispersions using spray techniques and to compare the physical-mechanical properties of the sprayed films to cast films. Aqueous dispersions of acrylic resin and cellulosic polymers were employed as the film forming materials.

EXPERIMENTAL

Materials

The following materials were employed as film-forming agents: methacrylic acid-ethyl acrylate copolymer aqueous dispersion (Eudragit® L 30D, Röhm Pharma, Darmstadt, Germany), ethylcellulose aqueous dispersion (EC, Aquacoat®, type ECD-30, FMC Corp., Newark, DE), cellulose acetate phthalate (CAP, Aquateric®, type CD901, FMC Corp., Newark, DE), and hydroxypropyl methylcellulose acetate succinate (HPMCAS, Shin-Etsu AQOAT®, type AS-MF, Shin-Etsu Chemical/Biddle Sawyer Corp., New York). Triethyl citrate was obtained from Morflex, Inc., Greensboro, NC. Dibutyl sebacate and diethyl phthalate were obtained from Eastman Kodak Co., Rochester, NY.

Preparation of Aqueous Polymeric Dispersions

The formulations for the film preparations are listed in Table I. Four aqueous polymeric dispersions were used in the study. The plasticizers and their mixture ratios were selected from each manufacturer's technical information (19-22). A 10% HPMCAS dispersion, which is common for coating, was difficult to spray since it could not be atomized through the spray nozzle. Therefore, a 5% dispersion was used in the spray method instead. The method of preparation for each dispersion included the addition of water and a plasticizer to each commercially available polymer. The following method was used to apply the plasticizers to each polymer: for Eudragit® L 30D, triethyl citrate was added to the dispersion, which was stirred for 2 hours. Gutiérrez-Rocca (23) reported rapid partitioning of the water soluble plasticizers, triethyl citrate and triacetin, with Eudragit® L 30D. Adsorption studies carried out to 72 hours did not demonstrate any increase in adsorption of these plasticizers to the polymer. To prepare the HPMCAS dispersion, the plasticizer was first dissolved in water at less than 20°C, and then polymeric powder added (20). The EC dispersion was prepared by adding the plasticizer and stirring the dispersion for 24 hours until visible droplets of the plasticizer disappeared. For the preparation of the CAP dispersion, polysorbate 80 was dissolved in water and the plasticizer was dispersed by homogenization with a Polytron® homogenizer (Brinkmann Instruments, Westbury, NY) for 15 minutes before the addition of the polymeric powder (21).

Preparation of Free Films

Cast Method. The dispersions were poured into leveled Teflon® molds (15 cm × 15 cm × 0.5 cm) and dried at 40° C for two days. The molds were then placed in a 100% relative humidity chamber for 10 hours for the acrylic films and 3 hours for the other polymers, to make the films flexible enough to be removed intact from the mold (10). The amount of dispersion used to prepare the films was quantified such that the resulting films had a thickness of approximately 200 μm for Eudragit® L 30D, HPMCAS, and CAP. As an EC cast film of 200 μm thickness was too fragile to remove intact, the thickness of this polymeric film was set at approximately 300 μm. After removal from the molds, the films were cut into 8 cm × 1.3 cm rectangular pieces with a surgical knife and stored in a constant humidity chamber maintained at 50% relative humidity and 23°C until the mechanical tests were performed.

Spray Method. The spray apparatus used in this study is shown in Fig. 1. The system consists of a spray gun with an atomizing-air supply system and a rotating drum. The aqueous dispersion was atomized by pressurized air. The atomized air also moved the liquid to the spray nozzle by siphoning from the sample bottle placed on a magnetic stirrer. Since a continuous spray would not give a uniform film, intermittent spraying was performed. The spray intervals were controlled by a solenoid valve connected with a programmable interval timer. From the gun (Badger, Model 350-IM, Franklin Park, IL), the dispersion was sprayed onto a Teflon® overlay (5 × 20 cm, Cole Parmer, Chicago, IL) attached to the drum (6.5 cm diameter) rotating at 100 rpm. The spray was performed by repeating a 10-second interval and 2-second spraying duration. The mean spray rate was approximately 1.5 g/min. Heated dry air was supplied to the cylinder surface, maintaining the temperature of the drum surface at 40°C. The distance between the spray nozzle and the cylinder surface was 30 cm, so that the spray pattern covered the whole area of the overlay. The amount of dispersion to spray was predetermined so that the resulting films had the same thickness as that of the cast films. After spraying, the overlays were removed from the drum and placed in a 100% relative humidity chamber for 3–10 hours,

Table I. Formulations of Aqueous Dispersions for the Preparation of Free Films

Polymer	Eudragit® L30D	HPMCAS (Shin-Etsu AQOAT®)	CAP (Aquateric®)	EC (Aquacoat®)
Solid content (wt%)	10	Spray: 5 Cast: 10	10	Spray: 10 Cast: 25
Plasticizer	Triethyl citrate	Triethyl citrate	Diethyl phthalate	Dibutyl sebacate
Placticizer content (wt% of solid)	20	28	35	24
Other ingredient			Polysorbate 80 3% of solid	

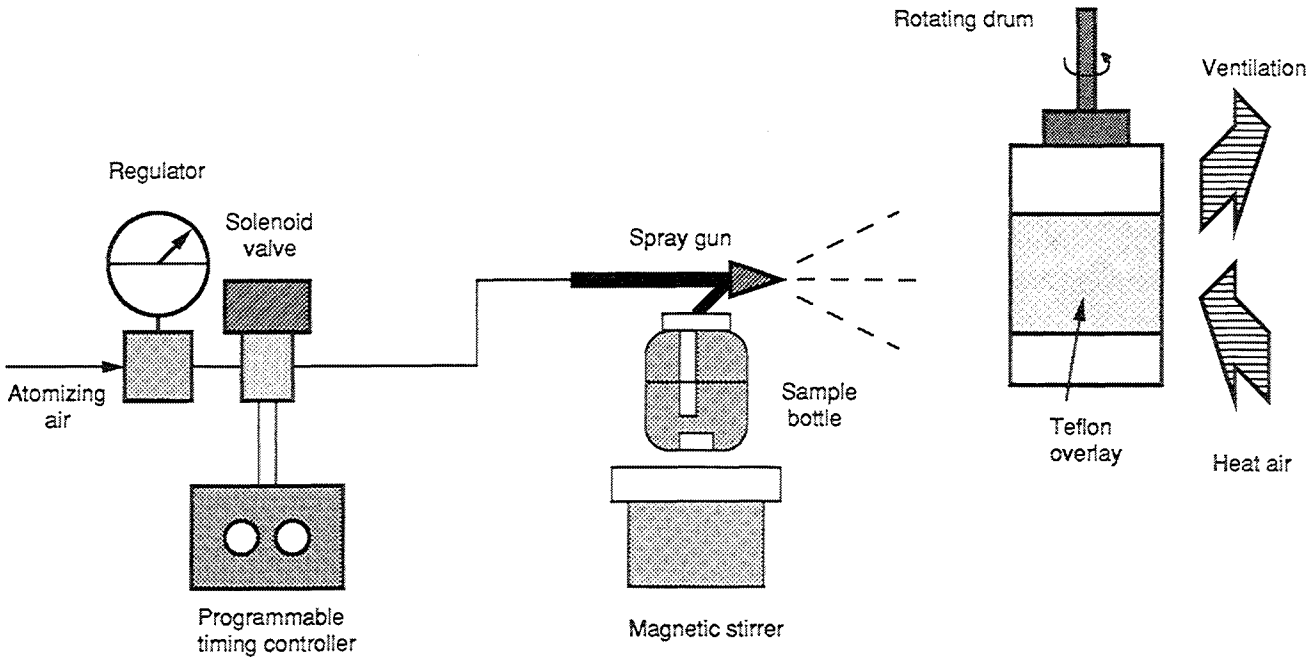

Fig. 1. Schematic view of spray system

depending on polymer, until they became flexible. This process also allowed the curved films to become flat. The polymer film was then removed from the overlay and cut in the same manner as described above. These film specimens were equilibrated for 24 hours in an oven maintained at 40°C, then stored in a 50% relative humidity chamber at 23°C until the mechanical tests were administered.

Mechanical Tests

The mechanical properties of the films were evaluated using an Instron Model 4201 universal testing apparatus. The rectangular film specimens (8 cm × 1.3 cm) were held in place with pneumatic grips, and the test procedure was based on the ASTM D882-75d method (24). The initial length of the film specimens was 40 mm, and the extension speed was 10 mm/min. Film specimens with physical damages were discarded. All samples were applied to the mechanical test one week after preparation. The test was carried out at 23 ± 2 °C and 50 ± 2 % relative humidity using a constant humidity chamber covering the entire Instron apparatus. The stress-strain curves were recorded for each sample, and the tensile strength at break, elongation, and elastic modulus were calculated.

RESULTS AND DISCUSSION

To prepare uniform and reproducible films by a spray method, it was important to use a spray gun which could produce small and uniform droplets. The spray gun used in this study was found to be suitable for free film preparation on a laboratory scale. In the present apparatus, a short tubing between the gun and the sample bottle was used to avoid sedimentation which might occur in the tube if a peristaltic pump with long tubing was used. This is an important consideration when spraying formulations containing solid ingredients such as opacifiers.

The data in Table II demonstrate the mechanical prop-

Table II. Mechanical Properties of Cast and Sprayed Films of Eudragit® L 30D

		Method	
	Evaluation	Cast	Spray
Tensile strength (MPa)	Within-run[1]	34.4 ± 6.2	31.5 ± 5.7
	Between-run[2]	31.0 ± 2.4	30.6 ± 2.6
Elongation (%)	Within-run	3.1 ± 0.8	3.4 ± 0.7
	Between-run	3.1 ± 0.7	3.3 ± 0.7
Elastic modulus (MPa)	Within-run	1447 ± 118	1381 ± 191
	Between-run	1304 ± 80	1372 ± 49

[1] Data represents mean ± standard deviation of at leat five film specimens from one preparation.

[2] Data represents mean ± standard deviation of at least five separate preparations. Mean values were determined from at least five specimens for each preparation and the standard deviation was calculated from those mean values.

Table III. Mechanical Properties of Cast and Sprayed Films of Hydroxypropyl Methylcellulose Acetate Succinate

		Method	
	Evaulation	Cast	Spray
Tensile strength (MPa)	Within-run[1]	4.5 ± 2.7	14.0 ± 1.6*
	Between-run[2]	5.2 ± 1.0	14.3 ± 1.2*
Elongation (%)	Within-run	6.6 ± 5.4	3.2 ± 1.0#
	Between-run	8.3 ± 2.5	3.0 ± 0.7#
Elastic modulus (MPa)	Within-run	298 ± 162	752 ± 104*
	Between-run	269 ± 80	785 ± 75*

[1,2] See Table II.
* Significantly different compared to cast films by Student's t-test ($P < 0.05$).
\# Significantly different compared to cast films by F-test ($P < 0.05$).

erties of the free films of Eudragit® L 30D. To evaluate reproducibility, "within-run" and "between-run" standard deviations were determined. Transparent films were obtained from this polymeric dispersion by both the cast and spray methods. The surface of the sprayed films had a slight rough texture due to small droplets of spray being deposited on the film surface. However, tensile strength, elongation, and elastic modulus of the sprayed films did not significantly differ from those of the cast films. Relative standard deviations of each mechanical value, for both within-run and between-run evaluations, were also similar. Therefore, the present spray method was found to be as reproducible as the cast method for this polymeric dispersion.

The mechanical properties of the HPMCAS films are shown in Table III. Marked within-run variation was observed for the elongation measurement with the cast films of this polymer. The value ranged from 2.6 to 17.9%. The difference between the within-run standard deviation of the two methods was statistically significant. There was also high within-run variation in elastic modulus. Sprayed HPMCAS films did not present such wide variation, for either the within-run or between-run evaluations. These results suggest that casting of this polymeric dispersion will result in uneven film formation. While the dispersing particles in the Eudragit® L 30D dispersions were stable for long periods, the HPMCAS dispersions were prepared by suspending micronized powder in water; thus the polymeric particles readily settled if not stirred continuously. In the present study, sedimentation was observed during the drying step after casting of these two polymeric dispersions. During the drying stage, film formation began at one position in the spread dispersion and gradually progressed throughout the plate. Simultaneously, water was expelled from the drying areas to the remaining wet regions of the spread dispersion. It is possible that this movement of water caused an uneven distribution of plasticizer in the film causing heterogeneous free film to form. The results suggested that the spray method was more suitable than the cast method for the preparation of uniform and reproducible free films from aqueous dispersions of HPMCAS. In the between-run evaluation, the tensile strength and elastic modulus of the sprayed HPMCAS films were approximately three times higher than those of the cast films. Although it was difficult to compare elongation determinations statistically due to the high variations seen with the cast films, the mean elongation of the sprayed HPMCAS films was lower than that of the cast films. Several reasons are proposed to account for these differences. Firstly, spray-dried particles can be entrapped in the film in the spraying technique (11), which can lead to hard and brittle films. In addition, the differences in drying rates will also affect the film structures. The film properties of HPMCAS have been reported for only solvent-based preparation (25). The reported tensile strength and elongation properties of the solvent-based cast films were closer to the aqueous cast films than the results obtained from the sprayed films that are reported in our study. This suggests that the structure of the organic cast films are more similar to the aqueous cast films than to the sprayed films for this polymer.

The mechanical properties of cast CAP films are seen in Table IV. While uniform films were obtained from the Eudragit® L 30D, HPMCAS, and EC dispersion by the spray method, film formation was not obtained from spraying the CAP dispersion. Since the casting of the CAP dispersion at 40°C resulted in transparent films, poor film formation by the spray method was not expected. Since film formation with this polymer did not occur from casting at 30°C, the minimum film forming temperature of this formulation was between 30°C and 40°C. An increase in air temperature to 60°C in the spray apparatus was also unsuccessful. A possible explanation for this result is that a rapid drying of the polymer may prevent a coalescence of the solid latex particles. Further investigation is required to elucidate this result. As shown in Table IV, wide between-run variations, similar to the cast HPMCAS films, were observed for elongation and

Table IV. Mechanical Properties of Cast Films of Cellulose Acetate Phthalate

	Evaluation	
Tensile strength (MPa)	Within-run[1]	2.8 ± 0.7
	Between-run[2]	2.8 ± 0.2
Elongation (%)	Within-run	18.8 ± 16.8
	Between-run	17.4 ± 4.4
Elastic modulus (MPa)	Within-run	88 ± 58
	Between-run	84 ± 18

[1,2] See Table II.

Table V. Mechanical Properties of Cast and Sprayed Films of Ethyl Cellulose

	Evaluation	Method	
		Cast	Spray
Tensile strength (MPa)	Within-run[1]	3.0 ± 0.5	4.0 ± 0.3*
	Between-run[2]	2.8 ± 0.4	4.0 ± 0.4*
Elongation (%)	Within-run	1.8 ± 0.4	4.5 ± 0.7*
	Between-run	1.7 ± 0.3	5.2 ± 0.5*
Elastic modulus (MPa)	Within-run	206 ± 12	202 ± 40
	Between-run	195 ± 15	181 ± 18

[1,2] See Table II.
* Significantly different compared to cast films by Student's t-test ($P < 0.05$).

elastic modulus. The elongation ranged from 3.1 to 45.0%. Since this polymeric dispersion was prepared by suspending the spray-dried powder in water, the particles would settle if not stirred. This settling of the particles resulted in uneven film formation from the CAP dispersions when prepared by the cast method. A similar result was found for the HPMCAS.

The results in Table V profile the mechanical properties of the EC films. The Aquacoat® dispersion displayed similar physical properties to Eudragit® L 30D, in that the sedimentation of the colloidal particles did not occur during the drying stage after casting. However, the surface appearance of EC films prepared by the cast method was influenced by the concentration of the solid. For solid concentrations of less than 15%, an "orange peel" appearance was seen throughout the entire film. An increase in the solid concentration improved the surface appearance of the film, and the 25% solid concentration was selected for further study. This dispersion produced smoother films, although cracks were still observed in some parts of the films. On the other hand, the spray method provided uniform films without any cracks even at a solid concentration of 10%. The results demonstrated that the spray method was a more suitable method than the cast method for the preparation of uniform films from this polymeric dispersion. As shown in the table, the variations in tensile strength, elongation, and elastic modulus were not significantly different between the cast and spray methods, both for the within-run and between-run evaluations. The sprayed EC films presented a significantly higher tensile strength and elongation than the cast films. As with other polymers, changes in the drying rate influenced film properties, and since cracks were readily formed in films prepared by the cast method, discontinuous structures will exist in the cast films. It has been reported that the mean film forming temperature of this dispersion is approximately 30°C at a similar plasticizer content (26). The drying and equilibrium temperature in this study was not far from the MFT. Thus it is possible that the coalescence was not completed under the present condition, which could lead to brittle films in the cast method. Different results would be obtained if compared under drying condition at higher temperature (18).

CONCLUSIONS

From this study, the following conclusions were made. For aqueous dispersions containing solid particles in which sedimentation occurs, casting is not a suitable method for preparation of free films, since heterogeneous films will result. The spray system used in this study can produce uniform and reproducible films from aqueous polymeric dispersions. The differences in the mechanical properties between sprayed films and cast films are polymer dependent. Eudragit® L 30D showed the same film properties for free films prepared from the cast and spray methods.

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